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CORRESPONDENCE

Letters to the Editor

On Being Critical of Implantable Cardioverter-Defibrillator Therapy

Tung et al. (1) are to be congratulated for their insightful and meticulous analysis of the literature of randomized trials of implantable cardioverter-defibrillator (ICD) therapy. There are 2 additional points that deserve amplification and to be made regarding the use of ICDs in clinical practice. First, a material weakness that cannot be minimized is that beta-blocker therapy was applied unequally in some of the ICD trials. For example, the 5% absolute improvement in survival that Epstein (2) points to as clinically important is almost matched (4.6%) by the beta-blocker carvedilol (3). This does not negate the conclusion that ICD therapy may prolong life (as Epstein points out), but it does cast some doubt on this conclusion.

This doubt, combined with other factors, has contributed to the use of the ICD in fewer than the predicted numbers of patients (4,5). Perhaps the most significant other factor limiting the use of ICDs is the presence of comorbid conditions in patients in the general population at a higher rate than the carefully selected patients in the randomized trial. Studies such as that of Hernandez et al. (5) exaggerate this underutilization of ICD therapy by applying findings from randomized trials to patients who were dissimilar (nearly 10 years older) to patients enrolled in trials and to patients who would have been excluded from such trials, for example, because of azotemia (4–6).

Difficulty in applying ICD therapy comes not only from concern about an overestimate of ICD benefit in appropriate patients, but also from the application of randomized trial data to the universe of patients, in whom the presence of multiple medical conditions would have led to their exclusion from such trials. In these patients, with other medical conditions competing as causes of death, the benefit of ICD therapy will likely be less and the potential for ICD harm may be greater (6).

The findings of underutilization of ICD therapy may well be the manifestation of the medical community agreeing with Tung et al. (1) in their assessment of the benefit of ICD therapy (7,8).

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Reply

We thank Dr. Stamato for his interest in our paper (1) and we echo his sentiments. We also appreciate the accompanying editorial by Epstein (2), which provided counterbalancing insights into this important issue. As electrophysiologists, we all share the common goal of optimizing and refining our current method of selecting at-risk patients who are most likely to benefit and least likely to suffer harm from implantable cardioverter-defibrillator (ICD) therapy. At present, our updated guidelines are indeed based on the best available evidence, although it is imperative that we keep these data in perspective. Our assertion regarding disparate low rates of beta blockade in the landmark trials was merely to illustrate that the net clinical benefit may have been amplified, but not to suggest that the entire benefit of ICD can be accounted for by beta-blocker inequity.

There are at least 2 degrees of separation that contribute to the difficulty in generalizing and applying ICD clinical trial data into the real world. First, there is the discordance between the inclusion criteria of a study and the actual population that is enrolled. As an example, the average enrolled ejection fraction is almost 10% less than the enrollment cutoff, although published guidelines are strictly based on inclusion criteria. This point is nicely reiterated by Myerburg (3) in his recent review on defibrillator usage after myocardial infarction.

Second, there comes the discrepancy between the actual enrolled population and the patient characteristics seen in the real world, thereby amplifying this generalizability gap. As Dr. Stamato points out, patients with noncardiac comorbidities, including advanced age, diabetes mellitus, peripheral vascular disease, renal disease, and pulmonary disease, tend to be under-represented in clinical trials. The potential futility of ICD efficacy in patients with chronic and end-stage renal disease has been suggested by multiple retrospective cohort analyses (4–8). Indeed, there exists a discrepancy in the real world between eligibility and implantation rates (9). Dr. Stamato may be correct in asserting that practicing